## Conservative treatment options for carpal tunnel syndrome: a systematic review of randomised controlled trials

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# Conservative treatment options for carpal tunnel syndrome: a systematic review of randomised controlled trials

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**Abstract** Carpal tunnel syndrome (CTS) is a common disorder, for which various conservative treatment options are available. The objective of this study is to determine the efficacy of the various conservative treatment options for relieving the symptoms of CTS. Computer-aided searches of MEDLINE (1/1966 to 3/2000), EMBASE (1/1988 to 2/2000) and the Cochrane Controlled Trials Register (2000, issue 1) were conducted, together with reference checking. Included were randomised controlled trials evaluating the efficacy of conservative treatment options in a study population of CTS patients, with a full report published in English, German, French or Dutch. Two reviewers independently selected the studies. Fourteen randomised controlled trials were included in the review. Assessment of methodological quality and data-extraction was independently performed by two reviewers. A rating system, based on the number of studies and their methodological quality and findings, was used to determine the strength of the available evidence for the efficacy of the treatment. Diuretics, pyridoxine, non-steroidal anti-inflammatory drugs, yoga and laser-acupuncture seem to be ineffective in providing short-term symptom relief (varying levels of evidence) and steroid injections seem to be effective (limited evidence). There is conflicting evidence for the efficacy of ultrasound and oral steroids. For providing long-term relief from symptoms there is limited evidence that ultrasound is effective, and that splinting is less effective than surgery. In conclusion, there is still little known about the efficacy of most conservative treatment options for CTS. To establish stronger evidence more high quality trials are needed.

**Key words** Conservative therapeutics · Carpal tunnel syndrome · Review literature · Randomised controlled trials

## Introduction

Carpal tunnel syndrome (CTS) is a compression neuropathy of the median nerve at the wrist. Any condition that reduces the size of the carpal tunnel or increases the volume of its content will cause compression of the median nerve. Symptoms of CTS include (nocturnal) pain, paraesthesias and hypaesthesias in the hand, in the area innervated by the median nerve. The estimated prevalence of clinically and electrophysiologically confirmed CTS in the general population is 2.7 % [3].

To relieve the pressure on the median nerve (directly or indirectly), several treatment options, both surgical and conservative, are available. The most common conservative measures for the initial treatment of CTS are

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local and systemic steroids, non-steroidal anti-inflammatory drugs (NSAIDs), diuretics, pyridoxine and wrist-splints [12, 37]. In addition, yoga, chiropractics, ultrasound and laser treatment has been advocated. However, convincing evidence of the efficacy of these conservative treatment options has not yet been established.

Inflammation of the flexor tenosynovium (non-specific or due to rheumatoid arthritis) causes thickening of the synovium which, in time, may result in median nerve compression. Treatment with injections of corticosteroids into the carpal tunnel and the prescription of systemic steroids are both intended to reduce this tenosynovitis [35]. NSAIDs provide pain relief, and also suppress inflammation [7]. Oral diuretics reduce oedema in the carpal tunnel (accompanying pregnancy and inflammation) [30]. Some researchers consider that a deficiency of pyridoxine (vitamin $B_6$) causes CTS, and therefore supplemental oral pyridoxine is prescribed [16]. Others, however, suggest that the positive response to pyridoxine in CTS patients may actually be related to an unrecognised peripheral neuropathy (commonly associated with diabetes mellitus) [6]. Immobilisation of the wrist in a neutral position with a splint maximises carpal tunnel volume and minimises pressure on the median nerve [21]. Stretching of the arm, hand and fingers (yoga postures) possibly has a similar effect [19]. The contribution of manual therapy (chiropractics) in the healing process of CTS is not known [18]. Ultrasound is assumed to have thermal effects on the target tissue resulting in an increase in blood flow, local metabolism and tissue regeneration, and also reducing inflammation, oedema and pain [5], thereby facilitating the recovery of nerve compression. The non-thermal effects of laser presumably promote tissue healing in a similar way, but the underlying mechanism is still unclear [4].

The objective of this systematic review was to determine the short and long-term efficacy of the various conservative treatment options for relieving the symptoms of CTS.

## Methods

### Search and selection of studies

To identify publications, a search was made in MEDLINE (1/1966 to 3/2000), EMBASE (1/1988 to 2/2000) and the Cochrane Controlled Trials Register (2000, issue 1). A generic search for randomised controlled trials (RCTs) was made [11], combined with a specific search for CTS (using the keywords carpal tunnel syndrome, carp$ tunn$, carp$ syndr$, and tunn$ syndr$). In addition, the reference lists of all relevant publications were checked.

A study was included in the review if the following criteria were met: 1) the study population consisted of patients with CTS; 2) the efficacy of one or more conservative treatment options was evaluated; 3) the study was designed as a randomised controlled trial; 4) the results were published as a full report, written in English, German, French or Dutch.

Studies were selected by two reviewers (AG, RS) independently and disagreements were discussed to reach consensus.

### Assessment of methodological quality

Two reviewers (AG, MdK) independently assessed the methodological quality of all selected studies. Disagreements between the reviewers were identified, and discussed until consensus was achieved. The criteria list that was applied (Table 1) has been recommended by the Cochrane Back Review Group for systematic reviews in the field of musculoskeletal disorders [41]. This list was adapted for reviewing conservative treatment options for CTS with regard to prognostic indicators (c), description of interventions (d) and outcome measures (j). The list consists of items on internal validity (b1, b2, c, e, f, g, h, i, l, n, p), external validity (a, d1, d2, j, k, m1, m2) and statistical criteria (o, q). Criteria could be scored as positive ('yes'), negative ('no') or unclear ('don't know'). The quality score of the studies was based on the number of positive scores for internal validity.

### Data-extraction

Data from the articles were extracted independently by two reviewers (AG, MS) and recorded on a standardised form. Information was collected on participants (age, gender, duration of symptoms, clinically and/or electrophysiologically confirmed CTS, number of patients bi-

**Table 1** Criteria list for the assessment of methodological quality of RCTs evaluating the efficacy of conservative treatment options for CTS*

Patient selection
- a. Were the eligibility criteria specified?
- b. Treatment allocation:
  - 1) Was a method of randomisation applied?
  - 2) Was the treatment allocation concealed?
- c. Were the groups similar at baseline with regard to the most important prognostic indicators?

Interventions
- d. 1) Was the index intervention explicitly described?
  - 2) Was/were the control intervention(s) explicitly described?
- e. Was the care-provider blinded for the intervention?
- f. Were co-interventions avoided or similar for all groups?
- g. Was the compliance acceptable in all groups?
- h. Was the patient blinded for the intervention?

Outcome measurement
- i. Was the outcome assessor blinded for the intervention?
- j. Were the outcome measures relevant?
- k. Were side effects described?
- l. Was the drop-out/loss to follow-up rate described and acceptable?
- m. Timing follow-up measurements:
  - 1) Was a short-term follow-up measurement performed?
  - 2) Was a long-term follow-up measurement performed?
- n. Was the timing of the outcome assessment similar for all groups?

Statistics
- o. Was the sample size described for each group?
- p. Did the analysis include an intention-to-treat analysis?
- q. Were point estimates and measures of variability presented for the primary outcome measures?

* All criteria were scored yes (+), no (–) or don't know (?).
Criteria are related to internal validity (b1, b2, c, e, f, g, h, i, l, n, p), external validity (a, d1, d2, j, k, m1, m2) or statistics (o, q).
The operationalization of the criteria is available from the authors on request

laterally treated, number of patients or hands randomised), interventions (type, treatment schedule), outcome measures, timing of the follow-up measurements, and results (point estimates and measures of variability, number of patients or hands). Although data on all reported outcomes were extracted, outcome measures on symptoms (e. g. pain, percentage of patients with improved symptoms) were considered as primary outcomes, because these are of the greatest importance for patients [23, 27]. Information on side-effects was also recorded.

### Statistical analysis

The quantitative analysis (meta-analysis) was limited to studies that were clinically homogeneous, i. e. for which the participants, interventions, outcome measures and timing of the follow-up measurements were considered to be similar. Study results were combined, using a fixed effects model, or a random effects model if the studies were statistically heterogeneous. For studies that were clinically heterogeneous, or did not present the data in sufficient detail to enable statistical pooling, a qualitative analysis was performed. In that case a rating system was used, consisting of four levels of evidence, based on the number of studies, their methodological quality and their findings [42]:

Level 1. Strong evidence – provided by generally consistent findings in multiple high quality RCTs.
Level 2. Moderate evidence – provided by generally consistent findings in one high quality RCT and one or more low quality RCTs, or by generally consistent findings in multiple low quality RCTs.
Level 3. Limited or conflicting evidence – only one RCT (either high or low quality) or inconsistent findings in multiple RCTs, respectively.
Level 4. No evidence – no RCTs.

Conclusions (positive, negative or neutral) with regard to the findings of the studies were based on the statistical significance ($p < 0.05$) of the outcome measures on symptoms as assessed by the reviewers. Both short-term (≤ 3 months) and long-term (> 3 months) results were considered. If at least 75 % of the studies had a similar conclusion, the findings were considered to be consistent. An RCT was (arbitrarily) considered to be of high quality if at least 6 of the 11 internal validity criteria were scored positive. A sensitivity analysis was performed to examine the results when high quality was defined as scoring 5 or more, or 7 or more of the internal validity criteria positive.

## Results

### Search and selection of studies

Fourteen publications met the inclusion criteria, 11 of which were found in MEDLINE. Searching EMBASE and the Cochrane database resulted in the identification of 1 and 2 additional publications, respectively. No extra publications were found by reference checking.

### Methodological quality

Initially, the two reviewers agreed on 68 % of the methodological quality criteria. Almost all disagreements were due to reading errors (81 %) and the rest to differences in interpretation (19 %). After discussion, all disagreements were resolved. The results of the methodological quality assessment are shown in Table 2. Seven of the 14 studies were of high quality. Many studies reported on random treatment allocation, but failed to describe the exact procedure (b1) or state whether the method of randomisation was concealed (b2). Also, information on co-interventions (f) and compliance (g) was often lacking. The most prevalent methodological shortcomings were that the study groups were not similar at baseline (c), that the care-provider was not blinded (or that this was not mentioned) (e), that the drop-out/loss to follow-up rate was unacceptably high (l) and that no intention-to-treat analyses was performed (or this was unclear) (p). Furthermore, side effects often were not described (k) and the majority of the studies did not include a long-term follow-up measurement (m2).

### Efficacy of the conservative treatment options

Data from the trials were not statistically pooled, because studies were clinically heterogeneous with regard to participants (different inclusion/exclusion criteria), interventions and outcome measures (different symptoms measured). Furthermore, there was often only one study that evaluated a certain intervention or comparison of interventions, and the presentation of the data did not always make pooling possible. Instead, all the conclusions with regard to the efficacy of the conservative treatment options were based on the strength of the available evidence according to the pre-defined rating system.

The conclusions of the studies with regard to short- and long-term symptoms are shown in Table 2. Table 3 presents the study characteristics (participants, interventions and results).

#### Steroid injections

Three studies, 2 high quality and 1 low quality, were identified. One high quality RCT [9] assessed the effect of a steroid injection proximal to the carpal tunnel. After 1 month significantly more participants had improved in the intervention group than in the control group. After 3 months, however, only the participants who had improved after 1 month were asked if they needed further treatment. Therefore no conclusion can be drawn with regard to the difference in long-term improvement in symptoms between the groups [24]. The other high quality RCT [32] compared a local steroid injection (into the carpal tunnel) with an intramuscular steroid injection. The local injection provided symptom relief for significantly more patients than the intramuscular injection (after 1 month). However, the long-term difference between the groups could not be evaluated,

**Table 2** Methodological quality of RCTs evaluating the efficacy of conservative treatment options for CTS

| Reference | Contrast studied | Internal validity | | | | | | | | | | | Quality score* | External validity | | | | | | | Statistics | | Conclusion[1] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | b1 | b2 | c | e | f | g | h | i | l | n | p | | a | d1 | d2 | j | k | m1 | m2 | o | q | ≤ 3 months | > 3 months |
| Steroid injections | | | | | | | | | | | | | | | | | | | | | | | | |
| Dammers [9] | injection/placebo | + | + | + | + | ? | + | + | + | + | + | + | 10 | + | + | + | + | + | + | + | + | + | positive | unclear |
| Özdogan [32] | local/systemic injection | ? | ? | + | – | ? | + | + | + | – | + | + | 6 | + | + | + | + | – | + | + | + | + | positive | unclear |
| Girlanda [22] | injection/ placebo | ? | ? | + | ? | ? | + | + | + | ? | + | ? | 5 | + | + | + | + | + | + | – | – | – | unclear | |
| Ultrasound treatment | | | | | | | | | | | | | | | | | | | | | | | | |
| Ebenbichler [13] | 1.0/0 W/cm$^2$ | + | + | + | + | + | – | + | + | – | + | – | 8 | + | + | + | + | + | + | + | – | + | positive | positive |
| Oztas [33] | 1.5/0.8/0 W/cm$^2$ | ? | ? | + | ? | + | ? | + | ? | ? | + | ? | 4 | + | + | + | + | – | + | – | – | + | neutral | |
| Pyridoxine | | | | | | | | | | | | | | | | | | | | | | | | |
| Spooner [39] | pyridoxine/placebo | + | ? | – | + | ? | + | + | + | + | + | + | 8 | + | + | + | + | – | + | – | + | + | neutral | |
| Stransky [40] | pyridoxine/placebo/ nothing | ? | ? | ? | ? | ? | ? | + | + | – | + | – | 3 | + | + | + | + | – | + | – | + | + | neutral | |
| Other types of oral medications | | | | | | | | | | | | | | | | | | | | | | | | |
| Chang [8] | diuretic/nsaid/steroid/ placebo | + | + | + | + | + | ? | + | + | + | + | – | 9 | + | + | + | + | + | + | – | + | + | positive (steroid) | |
| Pal [34] | diuretic/placebo | ? | ? | – | ? | + | + | + | + | – | + | + | 6 | + | + | + | + | + | + | + | + | + | neutral | unclear |
| Herskovitz [25] | steroid/placebo | ? | ? | – | ? | + | ? | + | + | – | + | ? | 4 | + | + | + | + | + | + | – | – | – | neutral | |
| Other treatment options | | | | | | | | | | | | | | | | | | | | | | | | |
| Davis [10] | chiropractic/medical care | + | + | + | – | ? | ? | – | + | – | + | + | 6 | + | + | + | – | + | + | – | + | + | | |
| Garfinkel [19] | yoga/current treatment | + | ? | – | – | + | ? | – | + | + | + | ? | 5 | + | + | – | + | – | + | – | + | + | neutral | |
| Aigner [1] | laser/placebo | + | ? | – | – | ? | ? | + | – | + | + | + | 5 | + | + | + | + | – | + | – | + | + | neutral | |
| Garland [20] | splint/operation | + | + | ? | – | ? | ? | – | ? | + | + | – | 4 | + | + | + | + | + | – | + | + | + | | negative |

all criteria were scored yes (+), no (–) or don't know (?).

* number of internal validity criteria scored positive.

[1] positive conclusion: index intervention significantly ($p < 0.05$) more effective than the control intervention(s) in relieving CTS symptoms. neutral conclusion: no significant differences between index intervention and control intervention(s). negative conclusion: index intervention significantly less effective than the control intervention(s). unclear: differences between the groups were not evaluated. blank: no outcomes on symptoms or no short- or long-term follow-up measurement.

**Table 3** Characteristics of RCTs evaluating the efficacy of conservative treatment options for CTS

| Reference | Participants | Interventions | Results* |
|---|---|---|---|
| Steroid injections | | | |
| Dammers [9] | mean age 52 years, 83% female, mean duration of symptoms 29 months clinical and electrophysiological CTS | (1) steroid injection (40 mg methylprednisolone, 10 mg lidocaine) proximal to the carpal tunnel (n = 30 patients) (2) placebo injection (10 mg lidocaine) (n = 30 patients) | Improvement in symptoms in 77 % (1) and 20 % (2) after 1 month (difference 57 % [95 % CI 36 to 77] ). No side effects in either group. |
| Özdogan [32] | mean age 46 years, 100 % female, mean duration of symptoms 38 months clinical CTS only Idiopathic CTS | (1) steroid injection (1.5 mg Celestone R) into the carpal tunnel and placebo injection (0.5 ml saline solution) into the deltoid muscle (same side) (n = 18 patients) (2) steroid injection (1.5 mg Celestone R) into the deltoid muscle and placebo injection (0.5 ml saline solution) into the carpal tunnel (same side) (n = 19 patients) | Improvement in symptoms in 50 % (1) and 16 % (2) after 1 month (difference 34 % [95 % CI 6 to 63]). |
| Girlanda [22] | mean age 45 years, 81 % female, mean duration of symptoms 53 months clinical and electrophysiological CTS idiopathic CTS 21 out of 32 patients bilaterally treated | (1) steroid injection (15 mg methylprednisolone acetate) into the carpal tunnel, repeated after 1 week (n = 16 patients/27 hands) (2) placebo injection (15 mg saline solution) (n = 16 patients/26 hands) | Improvement in paraesthesias, nocturnal acroparaesthesias, pain and motor deficit after 1, 2, 4, 8 weeks in (1) versus improvement in paraesthesias (after 1, 2 weeks), nocturnal acroparaesthesias (after 1, 2, 4, 8 weeks) and pain (after 1 week) in (2). Differences between the groups were not evaluated. No side effects in either group. |
| Ultrasound treatment | | | |
| Ebenbichler [13] | mean age 51 years, mean duration of symptoms 8 months clinical and electrophysiological CTS idiopathic CTS mild to moderate CTS all patients (n = 34) bilaterally treated | (1) ultrasound 1.0 W/cm$^2$ 15 minutes/session 5 sessions/week for 2 weeks, 2 sessions/week for 5 weeks (n = 45 hands) (2) placebo ultrasound 0 W/cm$^2$ (n = 45 hands) | Significantly more improvement in symptoms (pain, paraesthesias, sensory loss) in (1) versus (2) after 2 and 7 weeks, and 8 months. No side effects in either group. |
| Oztas [33] | mean age 52 years, 100 % female, mean duration of symptoms 84 months clinical and electrophysiological CTS idiopathic CTS 12 out of 18 patients bilaterally treated | (1) ultrasound 1.5 W/cm$^2$ 5 minutes/session 5 sessions/week for 2 weeks (n = 10 hands) (2) ultrasound 0.8 W/cm$^2$ 5 minutes/session 5 sessions/week (n = 10 hands) (3) placebo ultrasound 0 W/cm$^2$ (n = 10 hands) | Improvement in pain, pain/paraesthesias at night/day, frequency of awakening at night in both groups after 20 days, but no significant differences between the groups. |
| Pyridoxine | | | |
| Spooner [39] | mean age 43 years, 63 % female clinical and electrophysiological CTS idiopathic CTS | (1) pyridoxine 200 mg/day for 12 weeks (n = 18 patients) (2) placebo tablets (n = 17 patients) | Improvement in swelling and movement discomfort in (1) after 12 weeks, but no significant differences in swelling, movement discomfort, night discomfort and poor co-ordination between the groups after 12 weeks. |
| Stransky [40] | clinical and electrophysiological CTS | (1) pyridoxine 200 mg/day for 10 weeks (n = 6 patients) (2) placebo tablets (n = 5 patients) (3) no treatment (n = 4 patients) | Improvement in symptoms in 50 % (2), 80 % (2) and 75 % (3) after 10 weeks, but no significant differences between the groups. |
| Other types of oral medication | | | |
| Chang [8] | mean age 46 years, 73 % female clinical and electrophysiological CTS idiopathic CTS mild to moderate CTS | (1) diuretic (trichlormethiazide) 2 mg/day for 4 weeks (n = 20 patients) (2) NSAID-slow release (tenoxicam-slow release) 20 mg/day for 4 weeks (n = 22 patients) (3) steroid (prednisolone) 20 mg/day for 2 weeks, 10 mg/day for 2 weeks (n = 26 patients) (4) placebo tablets (n = 23 patients) | Significantly more improvement in the mean global symptom score (pain, numbness, paraesthesias, weakness/clumsiness, nocturnal awakening) in (3) versus (4) after 4 weeks. Minor side effects in 2 (1), 6 (2), 5 (3) and 3 (4) patients. |
| Pal [34] | mean age 47 years, 90 % female, median duration of symptoms 7 months clinical and electrophysiological CTS idiopathic CTS 33 out of 48 patients bilaterally treated | (1) diuretic (bendrofluazide) 5 mg/day for 4 weeks (n = 23 patients/41 hands) (2) placebo tablets (n = 25 patients/40 hands) | No improvement in symptoms at all in 54 % (1) and 50 % (2) after 4 weeks (difference 4 % [95 % CI – 18 to 25]). 1 patient with side effects in (1). |

**Table 3** Characteristics of RCTs evaluating the efficacy of conservative treatment options for CTS (cont)

| Reference | Participants | Interventions | Results* |
|---|---|---|---|
| Herskovitz [25] | mean age 50 years, 80 % female, mean duration of symptoms 21 months<br>clinical and electrophysiological CTS<br>1 patient with rheumatoid arthritis, 2 patients with diabetes mellitus<br>mild to moderate CTS | (1) steroid (prednison) 20 mg/day for 1 week, 10 mg/day for 1 week (n = 8 patients)<br>(2) placebo tablets (n = 10 patients) | Significantly more improvement in mean global symptom score (pain, numbness, paraesthesias, weakness/clumsiness, nocturnal awakening) in (1) versus (2) after 2 weeks, but no significant differences after 4 and 8 weeks. 3 patients with side effects in both groups. |
| Other treatment options | | | |
| Davis [10] | mean age 37 years, 59 % female<br>clinical and electrophysiological CTS<br>idiopathic CTS<br>58 out of 91 patients bilaterally treated | (1) chiropractic care (manipulation of soft tissues and bony joints of the upper extremities and spine) 3 treatments/week for 2 weeks, 2 treatments/week for 3 weeks, 1 treatment/week for 4 weeks, ultrasound 1.0–1.5 W/cm$^2$ 5 minutes for half of the chiropractic treatment sessions, nocturnal wrist supports (n = 45 patients)<br>(2) NSAID (ibuprofen) 3 x 800 mg/day for 1 week, 2 x 80 mg/day for 1 week, 800 mg as needed to a maximum of 2400 mg/day for 7 weeks, nocturnal wrist supports [n = 46 patients) | No outcomes on symptoms. 10 patients with side effects in (2) and 1 patient in (1). |
| Garfinkel [19] | mean age 49 years, 67 % female<br>clinical and electrophysiological CTS<br>idiopathic CTS<br>25 out of 42 patients bilaterally treated | (1) yoga (11 yoga postures for strengthening, stretching, balancing each joint in the upper body, and relaxation) 1–1.5 hours/treatment 2 treatments/week for 8 weeks (n = 22 patients/ 35 hands completed study)<br>(2) current treatment and wrist splint offered (n = 20 patients/32 hands completed study) | No significant differences in pain between the groups after 8 weeks. Improvement in sleep disturbance in 24 % (f) and 13 % (2) after 8 weeks (difference 11 % [95 % CI –14 to 36]). |
| Aigner [1] | mean age 54 years, 77 % female, mean duration of symptoms 29 months<br>clinical and electrophysiological CTS | (1) soft-laser light (Helium-Neon) 5 mV on 6 acupuncture points 15 seconds/point 2 treatments/week for 3 weeks (preoperative) (n = 13 patients)<br>(2) placebo laser acupuncture 0.5 V infra-red light (preoperative) (n = 13 patients) | Improvement in pain during the night in 100 % (1) and 69 % (2) after end of treatment/before operation (difference 31 % [95 % CI 6 to 56]). But no significant differences in improvement in paraesthesias and activity-associated pain between the groups after end of treatment/ before operation. |
| Garland [20] | mean age 47 years, 100 % female, mean duration of symptoms 4 months<br>clinical and electrophysiological CTS | (1) plaster-of-paris splinting of hand/wrist/arm for 1 month (n = 11 patients)<br>(2) open operation (n = 11 patients) | Significantly more relief of symptoms in (2) versus (1) after 1 year. No side effects in either group. |

* results of the outcomes on symptoms. p-values < 0.05 were considered to be significant.

because some patients received extra injections, and the moment of outcome assessment for them was different to that for patients who received no additional treatment. The low quality study [22] evaluated the efficacy of local steroid therapy (into the carpal tunnel), but differences in outcomes between the intervention group and the placebo group were not evaluated.

There is therefore limited evidence (level 3) that a steroid injection proximal to the carpal tunnel is more effective than placebo in improving CTS symptoms in the short-term (1 month). The same applies to a steroid injection into the carpal tunnel, compared with an intramuscular steroid injection.

## Ultrasound treatment

The efficacy of ultrasound was assessed in 1 high quality and 1 low quality RCT. In the high quality study [13], ultrasound treatment resulted in significantly more improvement in symptoms than 'sham' ultrasound in the short-term (2 and 7 weeks) and in the long-term (8 months). In the low quality study [33], no differences between the groups were reported in the short-term (20 days).

There is conflicting evidence (level 3) that ultrasound is more effective than placebo in relieving CTS symptoms in the short-term, and limited evidence (level 3) for its long-term effectiveness.

## Pyridoxine

In 1 high quality [39] and 1 low quality [40] RCT the effect of pyridoxine was evaluated. Neither study found any significant differences in symptom improvement between the treatment groups, indicating moderate evidence (level 2) that pyridoxine and placebo are equally effective.

### Other types of oral medications

Two high quality studies and 1 low quality study were found. One high quality RCT [8] assessed the efficacy of a diuretic, a NSAID, and an oral steroid, compared to placebo. Only the steroid group showed significantly more improvement in symptoms than the placebo group (after 4 weeks). In the other high quality RCT [34], no differences were found between a group receiving a diuretic and a placebo group (after 4 weeks). The long-term differences between the groups could not be evaluated, because only patients who improved after 4 weeks were assessed after 6 months. The low quality study [25] evaluated the effect of an oral steroid. After 2 weeks there was significantly more improvement in symptoms in the steroid group, compared with the placebo group, but this effect had disappeared after 4 and 8 weeks.

There is therefore strong evidence (level 1) and limited evidence (level 3), respectively, that diuretics and NSAIDs are not more effective than placebo. There is also conflicting evidence (level 3) that an oral steroid is more effective than placebo in improving CTS symptoms in the short-term.

### Other treatment options

The efficacy of chiropractic treatment (manipulation, ultrasound, wrist support) was compared with medical treatment (NSAID, wrist support) in 1 high quality RCT [10], but no outcome measures focussing on symptoms were included.

In 1 low quality study [19], a yoga-based regimen was as effective in relieving CTS symptoms as 'current treatment' (after 8 weeks). The control group did not receive uniform treatment, as they continued with their 'current treatment' (whatever that was), and were also offered a wrist splint. The authors falsely report that they assessed the efficacy of yoga compared with wrist splinting or no treatment [28], because the results of the study only indicate that there is limited evidence (level 3) that yoga is not more effective than 'current treatment'.

Only 1 low quality study [1] investigated whether soft-laser acupuncture was beneficial in the pre-operative treatment of CTS. The laser group had significantly more pain relief during the night, but did not have more relief from paraesthesias and activity-associated pain. Overall, there is limited evidence (level 3) that soft-laser acupuncture is not more effective in relieving symptoms than placebo.

Splinting was compared with surgery in 1 low quality study [20]. No short-term follow-up measurement was performed, but after 1 year splinting was found to be significantly less effective than surgery in providing symptom relief, indicating limited evidence (level 3).

### Sensitivity-analysis

Changing the cut-off point of the quality score to 5 or more, and 7 or more positive internal validity criteria, resulted in 10 and 4 high quality studies, respectively (Table 2). However, there was only one change in the level of evidence (from strong to moderate), namely that diuretics were equally effective as placebo, if high quality was defined as a positive score on at least 7 of the internal validity criteria.

### Side-effects

No side-effects were reported for steroid injections [9, 22], ultrasound treatment [13] and splinting [20]. Minor side effects (e. g. nausea, abdominal discomfort, headache) were reported for diuretics [8, 34], NSAIDs [8, 10] oral steroids [8, 25] and chiropractic treatment [10]. There was no information about the side-effects of pyridoxine, yoga or laser-acupuncture.

## Discussion

### Search and selection of studies

Because a few restrictions were made in the search, some studies could have been missed, which may have lead to bias. Unpublished studies and studies which were presented only in an abstract are more likely to have non-significant results [14, 36]. Furthermore, trials with significant results are more likely to be published in English [15].

### Methodological quality

There is no consensus on which criteria list should be used for assessing the methodological quality of RCTs. However, the criteria that are regarded as being most important in reducing bias, concealment of allocation and double-blinding, are included in the list used for this review [38]. The other criteria in the list are generally accepted methodological criteria that are also included in most of the other available lists [31]. In fact, the focus was on the quality of the reporting. It is possible that a trial did meet a certain criterion, but that for the sake of conciseness this aspect was not described in detail in the publication.

One drawback of combining information on different study characteristics related to internal validity into a sum-score for methodological quality is, that a positive score on one criterion might compensate a negative score on another. Therefore, a sum-score could conceal methodological shortcomings and variation in methods

between studies [26]. For this reason, the scores on each criterion for all studies are presented in Table 2.

### Efficacy analysis

Owing to the relatively small study populations, clinically relevant differences in outcomes between treatment could remain undetected. Statistical pooling would have increased the power, but it was decided not to pool the data and to perform a quantitative analysis, based on levels of evidence, instead. It is therefore possible that some smaller differences between treatment groups might have been missed. However, this does not seem likely when reviewing the data from the trials, because the differences that were not statistically significant were mostly so small that they were also not clinically relevant.

The strength of the evidence for the efficacy of an intervention is partly based on the methodological quality of the studies. The difference between high and low quality studies in this review was based on an arbitrarily chosen cut-off point, but varying this point had little influence on the results.

No consensus has yet been reached on how to assess the strength of the available evidence, and therefore the levels of evidence used in this review are, to some extent, arbitrary. It was decided to apply this rating system, because it has a good face validity, it is simple and explicit and had already been applied in several reviews on the effectiveness of conservative treatment options for low back pain [42, 43].

In a recently published Cochrane review on the effectiveness of local corticosteroid injections, it was concluded that injections result in greater clinical improvement in symptoms after one month, compared to placebo [29]. This review is comparable to the present review, and the results are based on two (high quality) trials that were also included in this review. The only difference is that no rating system for levels of evidence was used, but that the data were pooled (despite the fact that one trial compares a carpal tunnel injection proximal to the carpal tunnel with placebo and the other trial an injection into the carpal tunnel with an intramuscular injection). In a narrative review on the clinical management of (work-related) CTS [17], the conclusion was that there is limited evidence that steroid injections and pyridoxine are associated with pain reduction. However, the authors also state that this conclusion is preliminary because of the small number of controlled studies. This review differs from the present review in several ways: not only RCTs, but also other study designs were included, the methodological quality of the studies was not assessed and no rating system for the strength of the available evidence was applied.

The American Academy of Neurology recommends wrist splints, NSAIDs, diuretics and, at a later stage, steroid injections for the treatment of CTS. These methods of treatment are merely options, which implies that the recommendations are based on inconclusive or conflicting evidence or opinions [2]. According to the present review only steroid injections in, or proximal to the carpal tunnel might be effective in the short-term and ultrasound in the long-term, but the evidence is limited. Therefore, in the opinion of the authors, no clear recommendations can yet be made.

## Conclusions

There is still little known about the efficacy of most conservative treatment options for CTS. To establish strong evidence, there is a clear need for more high quality trials, not only focusing on the short-term, but also on the long-term effects, and providing adequate data.

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